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Transmissible spongiform encephalopathies:

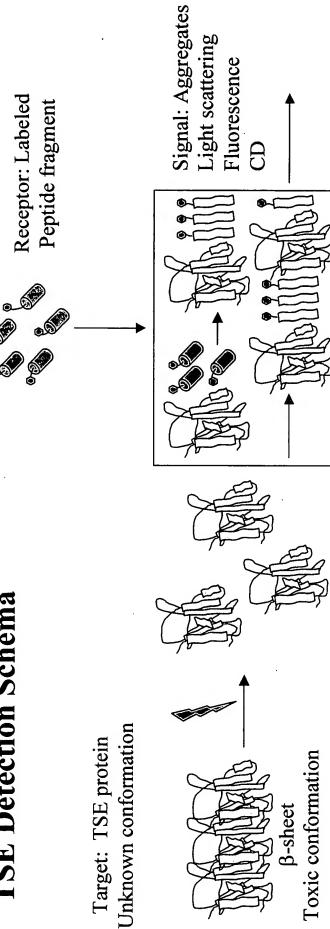
Labeled peptide β-sheet Toxic form TSE Conformers Non-toxic form α -helix

fragment

Figure 1

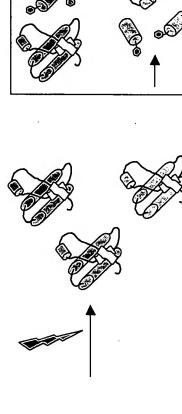
TSE Detection Schema

Target: TSE protein



Catalytic propagation

disaggregated



Non-toxic conformation

 α -helix

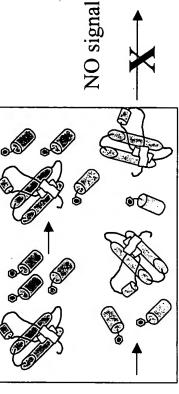
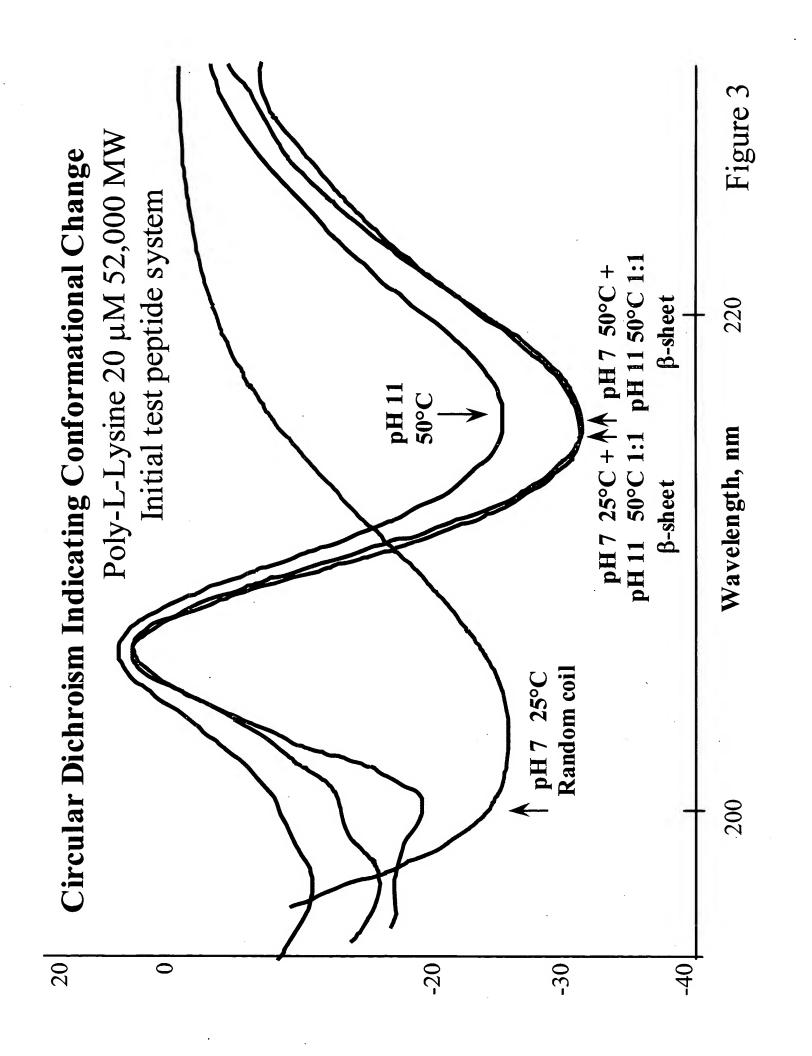


Figure 2



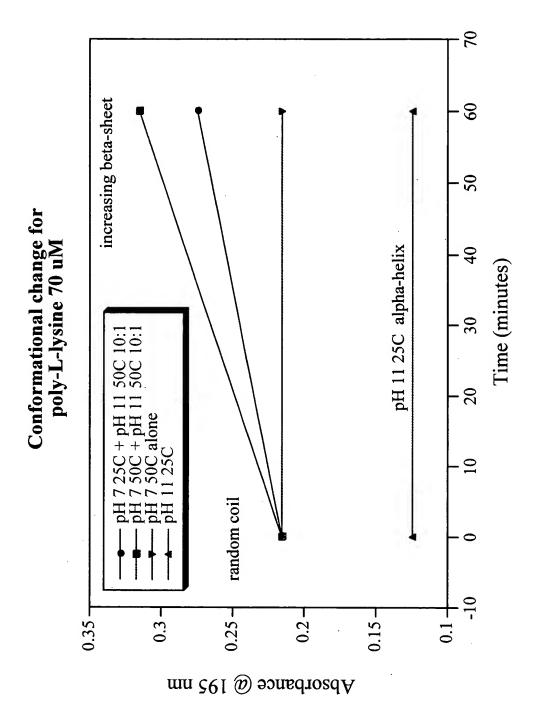


Figure 4

Circular Dicroism (CD) of Poly-L-Lysine varying Temp and pH

Temperature

25°C

 50° C

Random coil

pH 7 alone

Random coil

α-helix

pH 11 alone

B-sheet

B-sheet

B-sheet

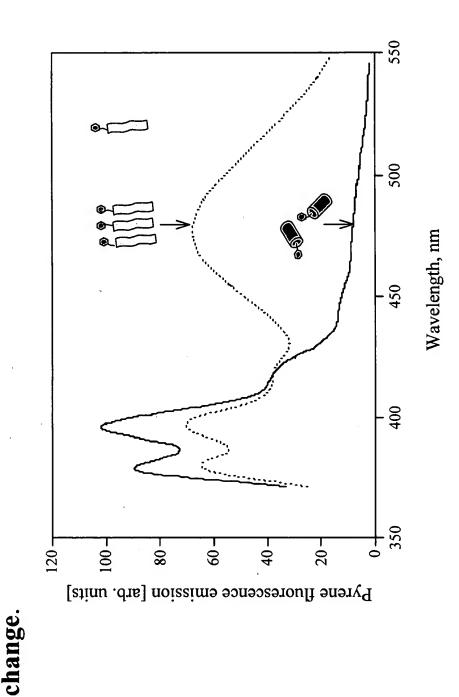
pH 7 + pH 11

Random coil

pH 11 25°C + pH 11 50°C

Figure 5

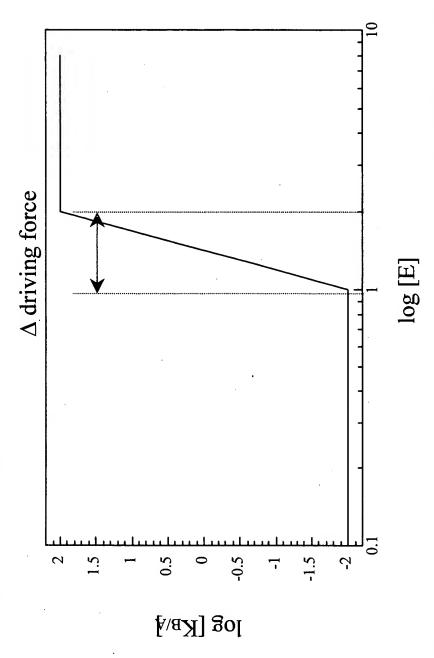
The data are from previous FRET experiments for proximal and distal locations in an α-helical bundle structure undergoing conformational Experiments with fluorescent probes for detection.



The spectra shown are for pyrene excimer formation at 480 nm, but other probes (FITC, etc.) can be used.

Figure 6

Engineering considerations for sensor design



The driving force must be commensurate with the energetic difference between the two conformational states

The process is driven by a differential interaction of the target peptide E, with the two conformations of the test PrP molecule.

Figure 7

Figure 8

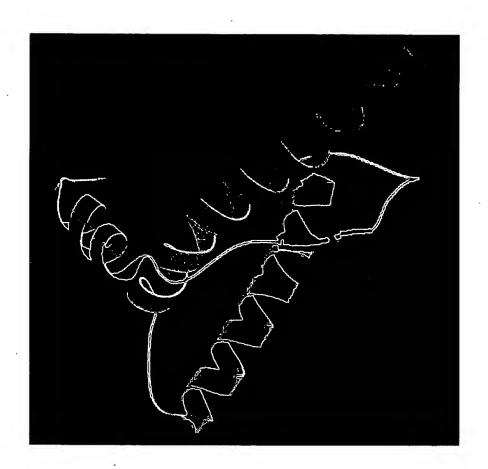


Figure 9

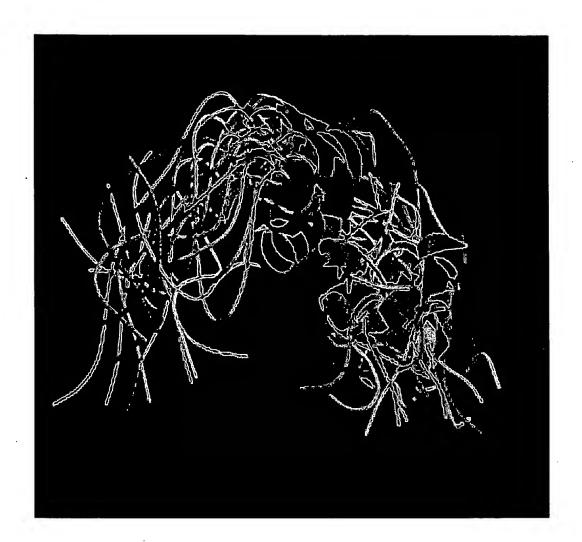


FIGURE 10

A.

33mer palindrome

VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV

19 mer KPKTNLKHVAGAAAAGAVV

14 mer LKHVAGAAAAGAVV

B.

TNLKHVAGAAAAGAVV

K

PKLKHVAGAAAAGAVV

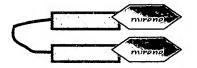


Figure 10. Palindromic 33mer peptide probe.

- A. Linear sequence of 33mer, 19mer and 14mer with palindromic sequences underlined and murine substituted V's and L's replace human/hamster sequence M's
- B. Folded sequence demonstrating parallel palindrome and diagram showing pyrene molecules present on both ends of the peptide forming an excimer structure.

